Cancer Nanotechnology Symposium
Nanotechnologies as Enablers of Breakthroughs in Cancer Early Detection and Therapeutics

National Cancer Institute Symposium

Weintraub Building
Fred Hutchinson Cancer Research Center
Seattle, WA

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Executive Summary

On March 4, 2004, the NCI held the third of what is expected to be a series of Nanotechnology Cancer Symposia whose primary purpose is to foster the interdisciplinary teamwork needed to leverage the promise of nanotechnology to detect, prevent and treat cancer. This symposium, *Nanotechnologies as Enablers of Breakthroughs in Cancer Early Detection and Therapeutics*, was held at the Fred Hutchinson Cancer Research Center (FHCRC) in Seattle, WA, and was hosted by Dr. Lee Hartwell, President and Director of the FHCRC and was chaired by Dr. Hartwell and Dr. Mauro Ferrari, Special Expert on Nanotechnology for the NCI and Professor of Biomedical Engineering and Internal Medicine at Ohio State University. The day-long meeting, attended by over 150 cancer biologists, engineers, chemists and oncologists from the FHCRC and investigators from other leading research institutions in the Seattle area, included lectures on cancer biology and nanotechnology, and produced an active exchange of ideas with the goal of developing a common understanding of nanotechnology and its potential applications to cancer. Additionally, the NCI sought input from symposia participants as the Institute puts the final touches on its Cancer Nanotechnology Plan (CNP), a strategic initiative aimed at rapidly translating promising nanotechnologies into clinical and research advances.

Two keynote speakers gave broad overviews of cancer and nanotechnology, with one lecture on the growing importance of genetically defined mouse models in studying cancer and developing target-specific diagnostics and therapeutics and the other outlining some of the different ways in which nanotechnology can impact cancer research and clinical oncology. The symposium featured talks on nanoscale laboratory-on-a-chip type applications that would benefit both basic research and cancer diagnostics, as well as nanodevices designed for *in vivo* and *ex vivo* use in deciphering cancer genomics and proteomics for diagnosing and characterizing cancer. Symposium speakers also discussed several different types of nanoparticles that could prove useful in creating multifunctional imaging, diagnostic and therapeutic devices, in addition to several presentations highlighting approaches that would quickly assess the efficacy of therapy. Presentations also delved into the materials aspects of nanodevices for biomedical use and further explored how genetically defined mouse models of cancer can serve as better test beds for novel nanodevices.

The ensuing roundtable discussions highlighted some of the important features needed from any nanoscale device developed for either research or clinical use. These included:

- identifying ways to monitor modifications of biological response during therapy, which could shorten the pathway to regulatory approval;
- developing and identifying new models for studying cancer;
- assessing the micro-environmental parameters of molecular expression that characterize the biology of cancer, including angiogenesis;
- detecting cancer and angiogenesis earlier in its natural history, either through imaging or serum-based detection;
- contrasting tumor tissue to normal tissue at important stages of tumor development; and
- detecting as early as possible if therapy is working.

The discussion also raised the notion that early detection was probably where the field could make the biggest impact, but that the clinical trials needed to prove that an agent capable of detecting presymptomatic cancer would probably be too long and too expensive to be feasible. In contrast, it should be possible to conduct clinical trials of agents designed to measure the efficacy of therapy simply by piggybacking on existing trials of new agents.

Introduction

If the Nation is to meet the 2015 goal of eliminating death and suffering from cancer, clinicians will need new ways to detect, treat and prevent cancer and metastases. One expectation of the field is that this era of post-genomic science, with its emphasis on genomic and proteomic analysis and systems biology, will generate unprecedented advances in knowledge, fostering paradigm-changing diagnostics, therapeutics and preventatives. At the same time, nanotechnology is rapidly making a mark among a small but growing group of NCI-funded cancer researchers as a disruptive set of tools capable of leveraging these scientific advances into a new generation of targeted clinical agents. Indeed, at least one nanotechnology based imaging product has demonstrated success in detecting micrometastases in humans and is awaiting FDA approval, and several other nanoparticulate imaging and therapeutic agents are showing remarkable promise in advanced animal models of cancer.

As a key component of its Cancer Nanotechnology Initiative, the NCI desires to boost the number of cancer researchers who are interested in applying nanotechnology to the problem of diagnosing, treating and preventing cancer. To help accomplish this, the NCI is holding a series of symposia aimed at introducing nanotechnology and its potential uses to as broad an audience as possible within the cancer and nanotechnology communities. An ancillary goal of these symposia is to solicit broad scientific input to provide direction to research and engineering applications and to identify barriers that are or may impede progress.

On March 4, 2004, the NCI convened the third of these symposia[1] at the Fred Hutchinson Cancer Research Center (FHCRC) in Seattle, WA, titled *Nanotechnologies as Enablers of Breakthroughs in Cancer Early Detection and Therapeutics*. Over 150 investigators from academia, industry and government participated in this symposium. Dr. Lee Hartwell of the Fred Hutchinson Salk Institute, who hosted the meeting, gave a brief introduction, explaining that the purpose of the day's proceedings was to solve a key barrier in applying nanotechnology to cancer research: most cancer biologists and clinicians do not know much about nanotechnology.

To set the stage for remaining talks, Dr. Mauro Ferrari, who shares a joint appointment with the NCI and the Ohio State University, first laid out the objectives of the meeting:

- Fostering exchange of information between cancer and nanotechnology researchers
- Facilitating regional self-assembly of multidisciplinary teams
- Obtaining conceptual feedback on strategic directions for integration in Cancer Nanotechnology Plan

He then presented the outlines of the Cancer Nanotechnology Plan, which as it currently stands is evolving along with three key components: extramural research, intramural research, and the soon to open National Standardization Laboratory (NSL). He also listed the seven challenge areas that the plan will address:

- Fundamental science, such as creating nanodevices that can pick up molecular signatures to provide the evolution over time of molecular signals and pathways;
- Prevention and control, such as bioengineered vaccines;
- Early detection, a key area, that will focus on topics such as enhancing mass spectroscopy-based proteomics and selectively harvesting molecules from blood and other tissues;
- Imaging, including developing injectable nanoparticles as targeted smart contrast agents that can simultaneously release therapeutics;
- Multifunctional devices, such as cellular factories and particles that can image, treat and report on the efficacy of treatment;
- Quality of life, which will examine using nanodevices to deliver medication to control pain, nausea and other side-effects, particularly in cancer patients whose cancers are beyond the help of therapy; and
- Cross-disciplinary training, which is central to meeting the other challenges

Dr. Ferrari elaborated further on the function of the NSL, which will create the ideal environment for the confluence of nanotechnology and cancer research, as well as providing the field with a facility that will develop multi-station protocols for validation, comparison, objective evaluation of nanodevices designed for eventual clinical use. The objectives of the NSL are three-fold: to develop multi-station protocols for validation, comparison, and developing indications for a wide variety of nanoscale materials; collaborate with the FDA to develop a rigorous, accelerated pathway towards clinical

[1] The first in the series, *Building the Interface of Nanotechnology and Cancer Imaging Research* was held January 28, 2004, in Bethesda, MD. The second in the series, *Nanotechnology: Visualizing and Targeting Cancer*, was held March 3, 2004, in La Jolla, CA.

translation; and to provide a place for the synergistic engagement of the private sector in developing cancer-directed nanotechnologies.

Cancer Biology and Nanotechnology Keynote Addresses

Dr. Douglas Hanahan of the University of California, San Francisco, spoke first, discussing two mouse models of multi-step, organ-specific carcinogenesis that closely mimic human cancer and showing how these models can inform drug development efforts. The first model, developed using RIP-Tag transgenic mice, showed three distinct stages of tumor development in pancreatic islets: hyperproliferation, angiogenesis, and tumor formation. Hanahan's team used this mouse model to answer three questions - can angiogenic switching be prevented, can tumor progression be slowed or stopped, and can tumor growth be stabilized or regressed and lifespan be extended – by trying to alter the transition between the three phases. Using a tyrosine kinase inhibitor that blocks the angiogenic switch, his research team showed that it could impair the growth of small tumors, but not cause regression of end-stage disease. In contrast, another inhibitor that blocks PDGF receptor was less effective against early disease, but had a marked effect on the last stage, leading to stable disease.

Using these probes in combination with the mouse model allowed the researchers to sort out the role that tumor cells, cells in the surrounding endothelium, and pericytes play in triggering the different stages of tumor development. These studies showed that PDGF receptor and VEGF receptors were involved in triggering and maintaining angiogenesis, but this involved production of those models by surrounding cells and not by the tumor itself. This finding led to a study giving both inhibitors, which had a more than additive effect that actually led to marked tumor regression. A followup study in which the investigators combined Gleevac, which targets the maintenance, or late phase, of angiogenesis by interfering with PDGF receptor, with a VEGF-receptor inhibitor that targets the early phase of angiogenesis again produced marked tumor regression by disrupting the tumor vasculature. Normal tissue vasculature was not affected. Dr. Hanahan concluded that since Gleevac is an approved drug, as is the anti-VEGF antibody Avastin, it may be pertinent to consider a clinical trial combining these two agents. It may also be pertinent to test Gleevec more broadly in tumors that themselves do not produce PDGF receptor.

In the second part of his talk, Dr. Hanahan discussed a mouse model of squamous carcinogenesis in the skin and cervix induced by the human papillomavirus (HPV). Coupling a particular set of genes from HPV with a promoter that targets expression to cells found in skin and uterine cervix, Hanahan and his team were able to develop a line of mice that spontaneously generate skin and cervical cancer. Using these mice, the investigators were able to study the importance of two enzymes involved in angiogenesis, matrix metalloproteinase genes MMP-9 and MMP-2. Both enzymes, the researchers found, increase in expression throughout tumor development, though they also found that MMP-9 is activated in surrounding stromal cells, too. Blocking this enzyme, either through knockout mutation or with a drug that inhibits the enzyme, impaired angiogenesis and the incidence and growth of tumors. In addition, these studies showed that macrophages infiltrating the tumor area are the primary source of MMP-9 and are

thus serving as functional enhancers – not inhibitors – of angiogenesis and tumor growth. But most importantly, these studies showed that MMP-9 inhibition must happen early during tumor development to have a positive effect, which could explain why clinical trials of MMP-9 inhibitors have gone poorly since they have been given to patients with advanced disease. Dr. Hanahan showed, however that zoledronic acid, a drug approved for others uses that coincidentally inhibits MMP-9, reduces vascularization in developing tumors and inhibits macrophage expression of MMP-9 and its protease activity, suggesting that a clinical trial in humans may show that this drug would work in the prevention phase of HPV-related cancer.

Dr. Hanahan closed his talk by showing how phage display techniques can identify peptides that home to the neovasculature of specific types of tumors, based on type of tumor and the organ they affect. These peptides may prove useful for conjugating with nanoparticles to deliver imaging contrast agents that would allow staging of neoplastic lesions in different organs and therapeutics that are specific for a given tumor in a given organ.

Dr. Samuel Wickline of Washington University in St. Louis then discussed how targeted, multivalent nanoparticles can facility a variety of innovations in diagnosis and therapy of cancer. This new class of agents should enable the *in vivo* characterization of the molecular mechanisms of disease using specific, high-affinity targeting ligands on polyvalent particles. They should also lead to targeted delivery of therapeutic agents and rational drug dosing with image-based guidance. Such nanoparticles should also provide the means to measure drug efficacy on the spot, yielding surrogate endpoints for more rapid evaluation of molecular therapies.

To illustrate the potential of engineered nanoparticles, Dr. Wickline discussed his team's work with lipid nanoparticles filled with perfluorocarbon. These particles can be "decorated" with targeting ligands, imaging contrast agents or therapeutics. He showed several examples of how these particles can be imaged using ultrasound, MRI and CT imaging, depending on the contrast agent added to the nanoparticle. He also showed an example of MRI-based cell imaging using a nanoparticle targeted to smooth muscle and to newly formed vasculature in a variety of tumor models. Dr. Wickline also demonstrated that it is possible to use fluorine NMR with nanoparticles containing ^{19}F-labeled perfluorocarbon to make quantitative measurements of how many nanoparticles are bound to their targets, which would provide data on local drug concentrations.

Dr. Wickline also showed how using a lipid-based nanoparticle offers unique opportunities for intracellular delivery of therapeutic or imaging agents. He showed the results of lipid labeling experiments that demonstrated exchange between the lipids in the nanoparticle and the cell membrane. As a demonstration of the utility of this property, he showed data from an experiment in which paclitaxol-loaded nanoparticles were capable of killing vascular smooth muscle cells only if the nanoparticles were targeted to those cells. He also showed similar data using targeted nanoparticles loaded with doxorubicin. Further studies showed that targeted nanoparticles were more effective at treating several

types of cancer in mouse models than free drug. Also, simultaneously measured MRI data predicted the degree of tumor response.

In closing, Dr. Wickline summarized the advantages nanoparticles can bring to imaging and therapeutic applications. With imaging, nanoparticles can increase sensitivity and specificity, detect disease earlier, and identify multiple disease mechanisms using multiple ligand and signaling molecules loaded onto the same nanoparticle. For therapy, nanoparticles provide the opportunity for increasing the dose of drug delivered to a targeted tumor or tissue while lowering drug toxicity and increasing the duration of action. Also, nanoparticles can include mechanisms for confirming and quantifying drug delivery and action. He then made several recommendations for the field. In the short term, he said, barriers to multidisciplinary research and collaboration must be lowered. He added that there is a need to expand efforts in signal quantification so that the results of therapy can be followed in close to real time over the duration of a given therapeutic protocol. Over the medium term, he argued that there is a need to focus on multispectral, polyvalent, targeted nanoparticles, involving ligand developers and pharmaceutical companies in these efforts. He voiced some concern that intellectual property issues may impede progress, and noted that getting one nanoparticle platform approved by the FDA for any imaging or therapeutic indication would have an energizing effect on the field.

Dr. Charles T. Campbell of the University of Washington, ended the keynote session with a brief overview of the research and development capabilities of the University of Washington/Pacific Northwest National Laboratory Joint Institute for Nanoscience and Nanotechnology, of which he is co-director. This facility, which recently became part of the National Nanotechnology Infrastructure Network, is a regional resource for any investigator who needs instrumentation for visualizing or characterizing nanodevices. Researchers at the laboratory are also conducting a wide range of biomedical research using nanotechnology, particularly in the areas of intracellular analysis and non-invasive imaging. He showed examples of using nanoscale technologies to determine single cell protein fingerprints, provide spatially resolved stimuli to single cells, perform *in vivo* high-resolution non-invasive optical biopsy of neoplasia, conduct high-throughput studies of protein-DNA interactions, and enable real-time quantitative PCR to detect minimal residual cancer.

Session 1: Foundations in Laboratory Research

Paul Yager of the University of Washington began the next session by discussing his team's work on developing inexpensive, disposable lab-on-a-chip devices that can rapidly conduct *in vitro* diagnostic tests, primarily using immunoassays. These devices, which he envisions as part of a distributed diagnosis and home healthcare system, are aimed at working with blood, saliva and other biological samples, and would be inserted into a "black box" device for analysis in a doctor's office in real time. Dr. Yager predicts that nanodevices will contribute to this effort by rapidly concentrating analytes at or near a detection surface and by directly coupling analyte binding to detection, sending a signal that binding has occurred.

In the cancer area, he predicts that this type of system will enable population-wide screening for genetic predispositions for cancer and monitoring pre-symptomatic phases in genetically susceptible individuals. Other uses will include optimization of chemotherapy, evaluation of therapeutic efficacy, monitoring chronic or critical drug treatment, and providing early warnings for emergent health conditions associated with therapy.

The heart of this system, as Dr. Yager envisions it, will be a disposable polymeric laminate cartridge that uses easily accessible samples without preconditioning. It will cost less than $5, hold all the chemistry needed for 20 or more different quantitative bioassays on a single drop or two of biological fluid, and be as rugged as a credit card. It will require only water to operate, it will insert into a handheld device, and provide laboratory-quality quantification of analytes in under five minutes. Current versions of the basic system being tested in his lab are approaching these ideals, but still require miniaturization. Reagents for each immunoassay will be stored dry in a matrix of complex carbohydrates that will be reconstituted as sample flows across a cavity holding the reagents. Experiments have shown that the rate of dissolution is controllable by altering the carbohydrate matrix, generating a constant plume of reagent as sample flows through it. Development work is also focusing on using surface plasmon resonance microscopy to measure immunochemical reactions.

Dr. James Olson of the FHCRC then discussed efforts to use nanotechnology to determine how effective a given anticancer therapy is within days or even hours of its use, rather than the months now required. Reducing this time gap is critical, he said, because the delay between drug administration and proof of efficacy can often leave patients with no further treatment options if therapy has failed. Addressing this problem would also shorten the time for completing clinical trials, which is particularly important for rare cancers where the number of drugs awaiting human clinical testing can easily exceed the capacity of the clinical trials system to recruit patients.

His approach to this issue is to develop nanotechnology capable of measuring apoptosis triggered by successful chemotherapy. Experiments to date show promise in using nanoparticles that detect a particular apoptotic protein, known as annexin V, using magnetic resonance imaging (MRI). Dr. Olson also discussed his group’s work on developing nanoparticles that can “paint” the edges of a tumor, which would enable surgeons to ensure that they had excised all of a tumor. He showed the results of using labeled and targeted nanoparticles and a combination of MRI and near infrared spectroscopy to outline the demarcation between tumor and healthy tissue in a mouse surgical model.

In the final presentation of the morning, Dr. Albert Folch of the University of Washington discussed how nanotechnology can create platforms on which researchers can conduct cell biology on a chip. These nanoplatforms can be constructed to accurately mimic the microenvironment in which a particular cell normally grows, producing a system capable of both perturbing cells and recording their responses in a manner more representative of how those cells would behave in the body than is observed in cells

grown in standard tissue culture systems. As a research tool, such systems would improve the reproducibility of current cell culturing systems while lowering the cost studying cells in culture.

The success of creating such a system lies with creating a nanofluidic chip that mimics the microenvironment in which a cell normally lives. Such a microenvironment includes channels through which nutrients and external signals can flow to cells, a feature that nanofluidic systems, by their very nature, reproduce. Because each microfluidic channel can be manipulated independently, growing cells over these channels affords the opportunity to control the microenvironment of single cells and to manipulate large numbers of cells in parallel using physiologic amounts of reagent. Dr. Folch discussed how his research team creates such surfaces and presented data showing how cells grow and differentiate in patterns defined by the microfluidic channels on the prepared surface. He also showed examples of using these cell biology chips to study axon guidance and for conducting high-throughput screening on arrayed cells.

Session 2: Transition to Imaging and Therapeutics

After a lunchtime discussion of NCI technology funding opportunities, led by the NCI's Ed Monachino, Dan Gallahan, Paul Wagner, and Avi Rasooly, who also holds a joint appointment with the Food and Drug Administration (FDA), symposia attendees were given a brief overview of the Washington Nanotechnology Initiative (WNI) by Keith Ritala of the WNI. The WNI, which got its start last year, began its mission of working with a nanotechnology community of researchers, business and investment people, and public sector groups to assess the state's opportunities in nanotechnology and to develop a strategy to nurture that industry and secure resources needed to implement that strategy.

Symposium attendees were then treated to three talks that gave an exciting view of how nanotechnology will help create novel cancer diagnostics and therapeutics. Dr. Constance Lehman of the University of Washington and the Seattle Cancer Care Alliance spoke of the need for new ways of diagnosing breast cancer early and for more effective therapies for advanced disease that has escaped early detection or failed to respond to a first line of treatment. She cited supporting statistics showing, first, that deaths from breast cancer are decreasing even though the incidence is increasing, largely because of earlier detection, and second, that five-year survival rates for breast cancer patients drop dramatically with later initial detection of disease.

Dr. Lehman suggested that there are two areas in which nanotechnology could dramatically affect breast cancer detection. The first would be to provide new methods for identifying cancer-associated biomarkers that will identify patients at risk before they develop overt breast cancer. The second will be to provide a more accurate prediction and monitoring of response to therapy in patients with more advanced disease. She then discussed promising early results of efforts to use nanoparticles as MRI contrast agents for detecting breast cancer, as well as other work aimed at using proton magnetic resonance spectroscopy to identify patients who are not responding to therapy early in their course of treatment.

Dr. Buddy Ratner of the University of Washington addressed some of the technical challenges of engineering surfaces at the nanoscale in order to create new materials for detecting and diagnosing cancer. Surface interactions are critical in the development of cancer, so nanotechnologists, Ratner said, have to be creative when it comes to making surfaces that will be of use in studying and identifying cancer. He showed an example of how cells grow in a much more ordered and natural manner on a modified polystyrene surface compared to an unmodified surface.

As a representative of the materials science community, Ratner showed numerous examples of the many technologies available for preparing well-defined surfaces with a wide range of physical and chemical properties. He also discussed methods for producing surface-modified materials that will respond to external stimuli, including materials that could release drug after receiving an ultrasonic pulse, as well as the need to develop surface modifications that will render materials biocompatible and resist biofouling. He showed several examples of how materials prepared with well-defined nanoscale features can be used as research tools to measure binding interactions and visualize protein-protein recognition. In addition, he said, it may be possible to create materials that a surgeon could apply to region surrounding a tumor that would cause the body to wall off the tumor, starving it and rendering it unimportant.

In the final talk of the day, Dr. Norman Greenberg of the FHCRC discussed the role that genetically engineered mouse models of cancer can play in testing the fruits of nanotechnology development efforts. These mouse models, which develop spontaneous cancer that closely mimic specific human cancers, particularly in contrast to implanted tumor models, can provide more rigorous and realistic assessments of novel imaging, diagnostic and therapeutic nanodevices. Dr. Greenberg says that these models, if widely used, would dramatically speed the clinical development of new diagnostics and therapeutics for cancer and would also reduce the number of drugs that fail in human clinical trials. And because these mice develop tumors whose molecular heterogeneity reflects that seen in human cancers, these models represent one of the only ways to truly assess how well nanodevices can administer multiple therapeutics in response to multiple molecular signatures. As an example, Dr. Greenberg discussed his group's work with a mouse model of prostate cancer that shows all the genetic and histological features of human prostate cancer. This model, called the TRAMP model, is both p53-/- and Rb-/-, and it undergoes the same type of angiogenesis and metastasis as human prostate cancer.

Dr. Ferrari and Dr. Hartwell then led a roundtable discussion that identified several areas that would be well-served by cross-fertilization among nanotechnologists, cancer biologists and clinical oncologists. These included:

- identifying ways to monitor modifications of biological response during therapy, which could shorten the pathway to regulatory approval;
- developing and identifying new models for studying cancer;
- assessing the micro-environmental parameters of molecular expression that characterize the biology of cancer, including angiogenesis;
- detecting cancer and angiogenesis earlier in its natural history, either through imaging or serum-based detection;

- contrasting tumor tissue to normal tissue at important stages of tumor development; and
- detecting as early as possible if therapy is working.

The discussion also raised the notion that early detection was probably where the field could make the biggest impact, but that the clinical trials needed to prove that an agent capable of detecting presymptomatic cancer would probably be too long and too expensive to be feasible. In contrast, it should be possible to conduct clinical trials of agents designed to measure the efficacy of therapy simply by piggybacking onto existing trials of new agents.

Reflecting today's tight funding environment and the need for new ways to support innovative interdisciplinary research, several participants raised the possibility of involving philanthropic organizations in efforts to create interdisciplinary teams that are working on high-risk, high-payoff projects. It was suggested that the NCI might be able to help philanthropies identify those teams. Participants also strongly supported the planned role of the NSL and coordinating its efforts with those of various regional nanotechnology facilities.

Recommendations for NCI Action:

In the discussions that followed each presentation and in the question and answer period after each session and following the day's presentation, the following were identified as opportunities for the National Cancer Institute to seize upon immediately, over the next 1-3 years, and to pursue over a 3-5 year period:

- Immediately
  - Clearly define standards and nomenclature for nanotechnology
  - Establish appropriate multidisciplinary funding mechanisms
  - Establish infrastructure for producing sophisticated new capture molecules
  - Begin process of working with CTEP and FDA to define regulatory issues
  - Encourage greater collaboration between academia and industry

- Short term (1-3 yrs)
  - Establish easily accessible, rapid-response core facilities for nanotechnology
  - Develop manufacturing capability for large-scale production of nanoparticles and nanodevices
  - Determine which cancers are most vulnerable to earlier/more general genetic predisposition screening
  - Determine which cancers are most vulnerable to earlier/better diagnosis
  - Determine which cancers are most vulnerable to better therapeutic monitoring
  - Develop methodology capable of detecting fewer than one million cancer cells
  - Demonstrate efficacious nanoscale device that can target a specific tumor and deliver a therapeutic compound

- Medium term (3-5 yrs)

- Provide mechanism(s) for ensuring both rapid and sustained commercialization of needed (but disruptive) diagnostic technologies developed in NCI programs
- Achieve remissions in three solid tumors using a nanoscale device
- Demonstrate nanoscale sensor that can simultaneously monitor multiple changes in tumor biophysiology in real-time
- Identify meaningful radiosensitizers for use in a nanodevice